

### AMENDMENTS

Please enter the following amendments:

#### Amendments to the claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### Listing of Claims:

Claims 1.-3. (canceled)

4. **(currently amended)** A hybrid oligonucleotide ~~consisting of~~ comprising one or more deoxyribonucleotide POPS blocks, the POPS blocks comprising alternating phosphorothioate and phosphodiester internucleoside linkages, ~~and one or more~~ flanked by regions of at least two contiguous 2'-O-substituted ribonucleotides ribonucleosides, wherein the 2'-O-substituted ribonucleotides ribonucleosides are linked by internucleoside linkages selected from the group consisting of phosphodiester and phosphorothioate internucleoside linkages.

5. **(currently amended)** The hybrid oligonucleotide according to claim 4, having from 12 to 50 nucleotides.

6. **(currently amended)** The hybrid oligonucleotide according to claim 4, having from 17 to 35 nucleotides.

7. **(previously presented)** The hybrid oligonucleotide of claim 4, wherein the alternating phosphorothioate and phosphodiester internucleoside linkages are present in a ratio of from 1:3 to 3:1.

8. **(previously presented)** The hybrid oligonucleotide of claim 7, wherein the alternating phosphorothioate and phosphodiester internucleoside linkages are present in a ratio of about 1:1.

9. **(previously presented)** The hybrid oligonucleotide of claim 7, wherein the phosphorothioate and phosphodiester internucleoside linkages alternate in a manner selected from the group consisting of one-to-one, two-to-one, one-to-two, two-to-two and three-to-three.

10. **(currently amended)** The hybrid oligonucleotide of claim 4, wherein the ~~one or more~~ regions of 2'-O-substituted ~~ribonucleotides~~ ribonucleosides are linked by phosphodiester internucleoside linkages.

11. **(currently amended)** The hybrid oligonucleotide of claim 4, wherein the ~~one or more~~ regions of 2'-O-substituted ~~ribonucleotides~~ ribonucleosides are linked by phosphorothioate internucleoside linkages.

12. **(new)** The hybrid oligonucleotide of claim 4, wherein one or more of the 2'-O-substituted ribonucleosides is a 2'-halogen selected from the group consisting of 2'-Cl, 2'-Br, and 2'-F.

13. **(new)** The hybrid oligonucleotide of claim 4, wherein one or more of the 2'-O-substituted ribonucleosides is a 2'-O-lower alkyl group containing 1-6 saturated or unsaturated carbon atoms, wherein such alkyl group may be unsubstituted or substituted with a chemical group selected from the group consisting of halo, hydroxy, trifluoromethyl, cyano, nitro, acyl, acyloxy, alkoxy, carboxyl, carbalkoxyl, amino or a combination of two or more such chemical groups.

14. **(new)** The hybrid oligonucleotide of claim 4, wherein one or more of the 2'-O-substituted ribonucleosides is a 2'-O-aryl or allyl group containing 2-6 carbon atoms, wherein such aryl or allyl group may be unsubstituted or substituted with a chemical group selected from the group consisting of halo, hydroxy, trifluoromethyl, cyano, nitro, acyl, acyloxy, alkoxy, carboxyl, carbalkoxyl, amino or a combination of two or more such chemical groups.

15. **(new)** An inverted hybrid oligonucleotide comprising one or more regions of 2'-O-substituted ribonucleosides linked by phosphodiester and/or phosphorothioate internucleoside linkages, wherein the one or more regions of 2'-O-substituted ribonucleosides are flanked by regions of deoxyribonucleoside POPS blocks, the POPS blocks comprising alternating phosphorothioate and phosphodiester linkages.

16. **(new)** The inverted hybrid oligonucleotide according to claim 15, having from 12 to 50 nucleotides.

17. **(new)** The inverted hybrid oligonucleotide according to claim 15, having from 17 to 35 nucleotides.

18. **(new)** The inverted hybrid oligonucleotide of claim 15, wherein the alternating phosphorothioate and phosphodiester internucleoside linkages are present in a ratio of from 1:3 to 3:1.
19. **(new)** The inverted hybrid oligonucleotide of claim 18, wherein the alternating phosphorothioate and phosphodiester internucleoside linkages are present in a ratio of about 1:1.
20. **(new)** The inverted hybrid oligonucleotide of claim 18, wherein the phosphorothioate and phosphodiester internucleoside linkages alternate in a manner selected from the group consisting of one-to-one, two-to-one, one-to-two, two-to-two and three-to-three.
21. **(new)** The inverted hybrid oligonucleotide of claim 15, wherein the one or more regions of 2'-O-substituted ribonucleosides are linked by phosphodiester internucleoside linkages.
22. **(new)** The inverted hybrid oligonucleotide of claim 15, wherein the one or more regions of 2'-O-substituted ribonucleosides are linked by phosphorothioate internucleoside linkages.
23. **(new)** The inverted hybrid oligonucleotide of claim 15, wherein one or more of the 2'-O-substituted ribonucleosides is a 2'-halogen selected from the group consisting of 2'-Cl, 2'-Br, and 2'-F.
24. **(new)** The inverted hybrid oligonucleotide of claim 15, wherein one or more of the 2'-O-substituted ribonucleosides is a 2'-O-lower alkyl group containing 1-6 saturated or unsaturated carbon atoms, wherein such alkyl group may be unsubstituted or substituted with a chemical group selected from the group consisting of halo, hydroxy, trifluoromethyl, cyano, nitro, acyl, acyloxy, alkoxy, carboxyl, carbalkoxyl, amino or a combination of two or more of such chemical groups.
25. **(new)** The inverted hybrid oligonucleotide of claim 15, wherein one or more of the 2'-O-substituted ribonucleosides is a 2'-O-aryl or allyl group containing 2-6 carbon atoms, wherein such aryl or allyl group may be unsubstituted or substituted with a chemical group selected from the group consisting of halo, hydroxy, trifluoromethyl, cyano, nitro, acyl, acyloxy, alkoxy, carboxyl, carbalkoxyl, amino or a combination of two or more of such chemical groups.